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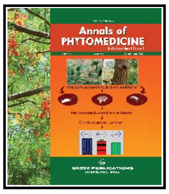



Review Article : Open Access

# A review on phytochemistry, pharmacology and ethnobotanical uses of *Cichorium intybus* L.

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**Abstract**

*Cichorium intybus* L. (chicory, Kasni) has been commonly used from long time as a coffee substitute, herbal drinks and as a salad. Several varieties are grown for the salad, roots are roasted and baked and used as a coffee substitute and in other beverages. From ancient times it has been used as a medicine for the cure of hepatic cancer, renal failure, diabetes, and others. It has several bioactive components including inulin, sesquiterpene, lactones, caffeic acid derivatives, coumarins, flavonoids, *etc*. Pharmacological activities ranging from antioxidant to cardioprotective, antihyperlipidemic, wound healing, antimicrobial, hepatoprotective and several others have been reported. In culinary uses, chicory can be used in various forms like, chicory flour, roasted chicory powder, chicory inulin, liquid chicory, roasted chicory cubes, instant chicory. The leading Indian brand Nestle, has already been using chicory in their product; Nescafe Sunrise. *C. intybus* (chicory) is valuable medicinal plant, further study needs to be done because many aspects of the plant have not been studied yet. The pharmacological activity of active chemical compounds isolated from the plant is proven only for a couple of activities, hence, it needs to be explored for other activities also. The main aim of this review is to critically analyze the *in vitro* and *in vivo* pharmacological activities, ethnobotanical uses, phytochemistry and other traditional applications of *C. intybus* and to cover the gap between previous and current studies thus, providing a platform for further future investigations.

## 1. Introduction

*Cichorium intybus* L. (*C. intybus*) commonly known as chicory or kasni, is a widely cultivated medicinally valuable herb belonging to the Asteraceae family. It is extensively harvested in several regions of Asia and Europe. Out of different species of chicory, *C. intybus* has been commonly utilized for various ailments since ancient times. Globally, *C. intybus* has been traditionally used as a medicinal plant, coffee alternative, salad, animal forage, *etc*. In the food industry, leaves and roots of chicory are used in the form of salad and vegetables, respectively. The roasted and baked roots of *C. intybus* is used in hot beverages as a coffee substitute. Roots are rich in inulin (Roberfroid, 2007) which is low in calories. It has been reported that the moisture content in chicory plants is 83%, crude protein 13%, crude fibre 2%, inulin 17%, total lipid 5%, carbohydrate 66% and ash 11%. Ethanolic extract showed 121.33 mg/100 g phenolic content of *C. intybus*, followed by acetone (102.44 mg/100 g), ethyl acetate (82.23), chloroform (52.56), aqueous (42.13) and hexane (14.23) (Khalil *et al*., 2019). *C. intybus* shows presence of over 100 active components including tannins, saponins, flavonoids, terpenoids, cardiac glycosides and anthocyanins, with majority of them present in roots. The roots are generally bitter and contain over 68% inulin. In addition, it also contains coumarins, flavonoids, sesquiterpene lactones (lactucin and lactucopicrin), tannins, alkaloids, vitamins, minerals, and volatile oils (Ali, 2020). It has several pharmacological properties as shown in Figure 1.

There are few limited numbers of detailed reviews reported on *C. intybus*. A detailed review covering the conventional uses, it's pharmacological and toxicology of *C. intybus* is available (Street, 2013). Another review is available on the medical importance of chicory (Al-snafi, 2016). This review is the first detailed review related to its phytochemistry, pharmacology and ethnobotanical uses.

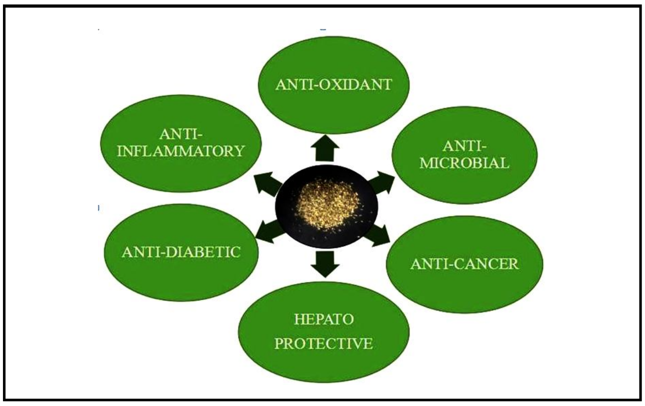


**Figure 1: Pharmacological properties of *C. intybus* plant.**

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## 2. Botanical description

There are six species in the *Cichorium* (Asteraceae) genus, primarily located in Europe and Asia, described by Bais and Ravishankar (2001). *C. intybus* L. is usually called chicory, is a perennial herb that grows up to 1 m tall with a fibrous taproot up to 75 cm long and big lower leaves (Bais and Ravishankar, 2001). Chicory has an extended historical usage in several ways, like it is used as a therapeutic herb, alternative of coffee and in various vegetable salad varieties and sometimes also used for animal fodder. It was seen in 1970, the content of inulin was 40% in chicory root, and it was also seen that it had no consequences on blood sugar thus, appropriate for people with diabetes (Judžentienė and Būdienė, 2008). Inulin is a fructose polymer that conserved cellulose in stem tubers, tuberous and taproots. Nowadays, *C. intybus* is being grown on an extensive scale to produce inulin (Van Arkel, 2012).

### 2.1 Morphology

*C. intybus* is commonly mentioned as chicory, is a type of herb which grows vertically and is usually rough and glandular in appearance. The length of bottom leaves are in between 7.5-15 cm, pinnatifid, and have serrated lobes, pointing downwards whilst the upper leaves are alternating. The length of stems ranges between 0.3-0.9 m, tilted or indented, branches are hard, inflexible, and spread radially (Bais and Ravishankar, 2001). Flowers of chicory are deep sky-blue in colour and they bloom from May through August. It is a capitate flower with a diameter of 3-4 cm and a bright bluish-purple (occasionally pink or white) appearance, radially symmetrical. The flowers are evenly-spaced along a dark-green, fibrous and inflexible stem. The leaves of this wildflower are divided into two types: huge dandelion-shaped leaves towards the stem's base and tiny lanceolate-to-oblong-shaped leaves along the stem's length (Mathur and Mathur, 2016).

### 2.2 Ecology/cultivation/harvesting

*C.intybus* may grow in soil, although it thrives in rich, deeply ploughed, high yielding soil or gardening soil when cultivated. It is a cool-weather crop that can only endure mild heat and necessitates evenly assigned rainfall with good sewerage or sprinkling in arid areas. For growing, *C.intybus* roots quickly and deeply, damp soil is insufficient. Compost is applied to the soil to neutralize its acidity and ensure proper root growth. It is susceptible to survive in the pH range of 4.5-8.3, yearly average temperature range of 6°C to 27°C and annual rainfall ranging from 30-400 cm (Duke, 1978; Duke, 1979).

The same cultural procedures apply to this root crop, the same as sugar beet. To allow root development, the soil depth should be ploughed down to 17- 25 cm. Seed should be sown onto a solid and smooth seedbed at a rate of 2.25 kg per hectare, depth 0.6 cm and a distance of 45-60 cm between them. The process of germination takes a long time because it grows slowly; the extra workforce required to suppress weeds can be avoided by planting it after some other crops like beans or maize. Planting could be started right away. Plants are thinned down when they reach the four leaf stage so that they may stand at a distance of 20-25 cm in the row. To avoid harming the taproot, the primary cultivation should be more profound than the future, which is sown comparatively less deep and distant from each other. Thinning should also not be done too late, since it may disrupt the roots of the remaining plants. Because bottom heat stimulates overly quick growth of the shoots, fertilizer should be mixed above the bed rather than underneath the roots. Seeds are scattered over the seedbed in some sections, and seedlings are trimmed in each direction to stand apart at a distance of about 25 cm.

The harvesting process could be delayed in the season as feasible, as roots typically grow in size and weight throughout the cooler months. Remnants of roots should be removed carefully when it gets established as weeds. The top part is cut down and either left to decompose as green manure or used as a forage. Then for further processing of *C. intybus* root, it is sent to the processing factory. Processing steps include washing of the roots, slicing into cubes, and drying over flame at the factory. Roots that has been dried can be kept indefinitely. The dried part is roasted and ground to a fine powder which is suitable for combining with ground coffee in the last step. The industrially processed products are shown in Figure 2. For daily life purpose, bulk powdered is typically sold out in waterproof container and in tiny packages also. *C. intybus* is harvested when the roots and leaves are at young stage of growth and its root are alleviated with the help of beet lifter and then plucked manually, at the end of summer. Pothole which is being covered with leaves are used for quick usage. The remnants are chopped off into 20-22 cm lengths and placed upright in the trenches, hotbeds, or other similar places to maintain a constant temperature of 15°C-21°C. After positioning the plants, so that their crowns are of the same length, 17-20 cm of dry loose soil is added. The marketable heads or chicons produced from *C. intybus* are formed around 12 to 20 days, with the most desirable heads measuring 10-15 cm in diameter and about of 0.06-0.09 kg of weight (Reed, 1976).

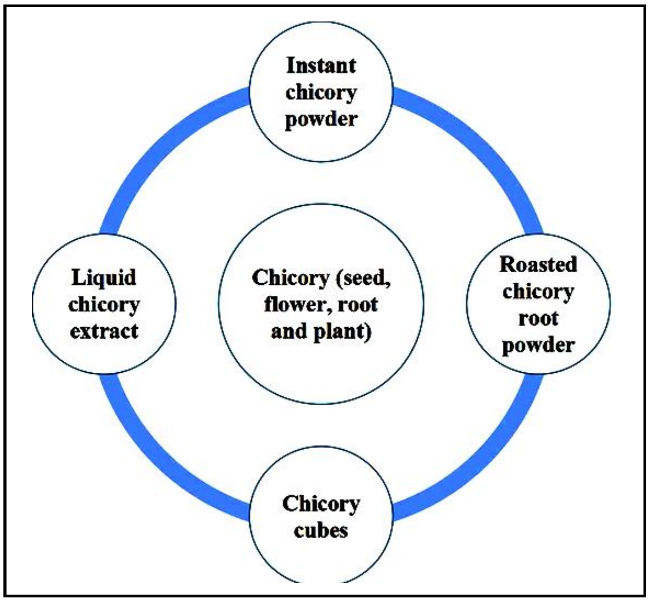


**Figure 2: Industrially processed product of *C. intybus* plant.**

## 3. Ethnobotanical aspect

### 3.1 Traditional culinary use

In Europe, *C. intybus* root has been grown for coffee consumption, especially in the Mediterranean region, baked and crushed roots are used as an addition (where this plant is native). It is also used as a coffee ingredient in the Indian variety of filter coffee, as well as in regions of Southern US, South Africa and South East Asia especially in New Orleans. Ricoré is a blend of 6:4 of chicory and coffee, which is offered in France. Its consumption peaked during periods of economic distress of the great depression during the period of 1930s and during World War IInd period and was exceptionally high. There was a coffee crisis in East Germany in 1976-79 and then chicory was introduced with rye and sugar beet. Palestinian, Lebanese, Turkish, Greek, and Syrian cuisines incorporate it in their coffee (web.archive.org).

Roasted chicory is used by some brewers to add coffee-like flavour into the beer. Some brewers have utilized chicory to complement the hops in strong blond Belgian-style ales, resulting in a witlofbier named after the plant's Dutch name.

#### 3.1.1 Inulin and chicory root

Inulin is a polysaccharide, and in chicory root, its content is 20%. It is found chiefly as a storage carbohydrate in plants of the Asteraceae family (such as Jerusalem artichoke, dahlia, and yacon). Food industries used inulin as an artificial sweetener and a prebiotic in yoghurt. It has a sweetening capacity of 10% of sucrose, and thus can be a suitable replacement for sugar. Among other things, inulin is gaining appeal as a soluble dietary fibre and functional food (Madrigal and Sangronis, 2007).

A nutritional ingredient or food additive made by mixing desiccated, crushed root of chicory plant along with water and then filtering and centrifuging the insoluble fraction out is known as chicory root extract or chicory root powder. Other techniques may be utilized to eliminate the colours and calories from the food. It is utilized as a reservoir of soluble fibre in various applications. Inulin 68%, sucrose 14%, cellulose 5%, protein 6%, ash 4%, and 3% other chemicals are found in fresh chicory root by dry weight. The amount of inulin in the root extract of dried chicory is 98% by weight, with just 2% of other compounds (Kim and Shin, 1996). When fresh chicory root is harvested, the inulin concentration can vary from 13 to 23% by weight (Wilson *et al.*, 2004).

Inulin and oligofructose are two sugars that are widely utilized in the food industry. Because of the variation in chain length between inulin and oligofructose, the functional characteristics of inulin and oligofructose are pretty different from one another. Solubility of inulin is less than oligofructose due to variation in its chain length, and when sheered in water or milk, it can produce inulin microcrystals, which are little crystals of inulin. These crystals are not noticeable in the mouth, but they work together to provide a creamy texture and a mouthfeel that is similar to that of fat. Inulin has been effectively utilized to replace fat in table spreads, baked goods, fillings, dairy products, frozen desserts, and salad dressings as a consequence.

Furthermore, fructans are non-cariogenic because Streptococcus mutants do not utilize them to produce acid or glucans, both of which are responsible for tooth decay. Shorter chain oligomers make up oligofructose, which possesses characteristics comparable to sugar and glucose syrups. It possesses 30% to 50% of the sweetness of regular use sugar and is more soluble than sucrose.

In cultivation, chicory roots are subjected to create two varieties: Barbe de capucine and witlof, during fall and winter season. The roasted roots which gives a bitter, mellow flavour is used as a coffee alternative. The leaves and roots of chicory are eaten as a vegetable or salad (Hammer, 2013).

### 3.2 Use in traditional and local cuisine and healthcare

In India, *C. intybus* is known as "kasni". It is utilized to treat acne, throat inflammation, spleen enlargement, diarrhoea, and vomiting on a local level (Jindal *et al.*, 1975). The polyphenolic group of compounds are associated with herbal chemical compounds that have been shown to possess medicinal and therapeutic properties (Kähkönen *et al.*, 1999; Pyo *et al.*, 2004). *C. intybus*, sometimes known as "chicory" has been used in the traditional medicine system for hundreds of years from North Africa to South Asia. Caffeic acids, cichoric as a monoester of quinic acid, and numerous flavonoids as iso-rhamantin are all found in the leaves. Cichoriolide A, cichorioside A, B, and C, as well as nine recognized sesquiterpene lactones, are found in the roots (Bais and Ravishankar, 2001). The bitter taste of chicory is primarily caused by sesquiterpene lactones (Ahmed *et al.*, 2003).

Another research examined the science behind several chicory root uses, such as chicory root juice for uterine cancer and tumour prevention, its tea for jaundice, and as a tonic and purifying medicine for newborns (Street *et al.*, 2013).

Chicory is currently used for a variety of purposes, including baking and grinding chicons or roots as a coffee alternative and supplement, eating chicory leaves as a vegetable, and growing chicory as a fodder plant for poultry and animal feed (Saeed *et al.*, 2017)

## 4. Other uses

### 4.1 Sources of fibre

Chicory is high in inulin, a soluble dietary fiber that is especially beneficial in non-ruminant feeding and is also used as a beneficial food component (Madrigal and Sangronis, 2007; Mejer, 2006; Roberfroid, 2004). Prebiotics have been proven in numerous studies to increase the growth of gut bacteria which is valuable for overall health, such as lactobacilli and bifidobacteria (Roberfroid, 2001; Kaur and Gupta, 2002). A prebiotic helps in boosting the immune system, thus reducing the harmful bacteria numbers in the colon (Liu *et al.*,, 2012), treat irritable bowel, and by improved mineral absorption it reduces the chance of osteoporosis (Roberfroid, 2002), particularly calcium ions, minimises the formation of triglycerides and fatty acids in the liver along with their serum levels, and thereby reduces the risk of atherosclerosis (Kaur and Gupta, 2002). When incorporated in male pig diets, probiotic inulin has been shown to diminish boar taint and foul-smelling chemicals in colon and their other parts (Van Loo, 2007; Jensen and Hansen, 2006; Rasmussen, 2012).

### 4.2 Animal feed

From ancient times, *C. intybus* was utilized as a medicinal plant, coffee substitute, and vegetable crop by the ancient Egyptians, and it was also used as animal fodder occasionally. A study revelaed that chicory is a plant that may be utilized as a source of fiber in pig diets (Ivarsson *et al.*, 2011). According to various research findings (Das *et al.*, 2016; Tzamaloukas *et al.*, 2006; Heckendorn*et al.*, 2006; Van Loo, 2007; Athanasiadou *et al.*, 2007), root of *C.intybus* is well known for its toxicity to internal parasites. Inulin feeding has been shown to reduce parasites such as Ascaris (Petkevičius *et al.*, 1997) and Trichuris (Thomsen *et al.*, 2005) in pigs since then. Decreasing the intestinal pH has been suggested as a possible mechanism, which is not suitable for the development of the parasitic embryo. Two different studies (Tzamaloukas *et al.*, 2006; Athanasiadou *et al.*, 2007) suggested that chicory as an ideal feed supplement for farm animals. The first study showed reduction in the worms to the chicory fed farm animals. The total helminths in the rennet bag of lambs grazing on *C.intybus* was observed to be significantly decreased in the second research done by Marley and Co-workers (2003). It was reported that chicory also include small amount of condensed tannins (Wilson *et al.*, 2004; Li *et al.*, 2005; Kidane *et al.*, 2010; Lombardi *et al.*, 2015) and sesquiterpene lactones (Miller *et al.*, 2011) which may impact the protein uptake efficiency in ruminants and reduces the number of parasites in animals intestine. It was observed that sesquiterpene lactones (SLs) in *C. intybus* extract suppressed the hatching of sheep's *Haemonchus contortus* eggs (Foster *et al.*, 2011). Previously, using a larval migration inhibition assay, some researchers (Molan *et al.*, 2003) discovered that *C. intybus* extracts high in condensed tannins and sesquiterpenes had a dose-dependent anthelminthic effect on lungworm and gastrointestinal nematode larval motility. *C. intybus* extract has been shown to possess a good effect on parasites as well as Lawsonia bacteria in pigs in Denmark (Roepstorff *et al.*, 2005), and it is very cheap, although it might induce intestinal obstruction if taken excessively.

### 4.3 Cosmetics

Chicory root extract is utilized in different skin formulations used in the cosmetic industries. According to a research, it was concluded that *C.intybus* root extract can improve skin barrier function by showing protective effects on skin. For this study, they chose 45-60 yrs old 50 females and divided into two groups. First group received the formulations with UV filters and another group received without any UV filter. At a time period of 14 and 28 days, transepidermal water loss and skin texture was recorded. It was seen that formulations containing the extract, decreased transepidermal water loss and improved skin microrelief as compared to the vehicle and control areas after a 28-day period (Maia Campos *et al.*, 2017). In continuiation with this research, a group of researchers also showed the instant and delayed effect of chicory root extract present in a cosmetic formulation. For this, 15 subjects were chosen and divided in to two groups. First one received formulations containing chicory root extract and another one received without it. For instant effect, measurement of certain skin parameters like transepidermal water loss and microrelief were observed just after 2 h, and for long term or delayed effect, it was measured after 45 and 90 days. The researchers concluded that only the chicory extract containing formulation was effective against sking barrier function and skin hydration. Thus, chicory extract can be used in cosmetic industries (Paseto *et al.*, 2017).

Extracts of *Spirulina*, *Palmaria palmata*, *C. intybus*, and *Medicago sativa* have also been studied and used in cosmetic compositions (Campo *et al.*, 2019). According to research findings, these extract showed no cytotoxicity and also showed *in vivo* acceptibility. The results showed no harmful effect against skin barrier and other skin related parameters. Thus, findings suggest that these extracts can be safe to use in cosmetic formulations.

### 4.4 The current importance of *C. intybus*

It is widely used in the food and beverage business, in addition to its usage in traditional medicine for various disorders such as liver disorder, renal disorder, diabetes, and so on. *C. intybus* root that has been roasted is commonly used as a coffee alternative. It has no or very little caffeine, which is why it is used to reduce inulin intake. This coffee was popular during WWII in the 1940s, and it has recently regained appeal due to its beneficial properties and bitter taste. Since chicory coffee is a caffeine-free coffee, therefore, its is being used as a coffee substitute, making it a healthier alternative to normal coffee.

According to the findings, the chicory export market has shown a significant increase in both quantity and value terms. The worldwide chicory market was anticipated to be worth $685 million in 2020, and is expected to grow at a CAGR of 5.7 per cent to$ 905 million by 2025.The chicory market in the United States is expected to reach $5.09 billion in 2026, growing at a CAGR of 2.62 per cent from 2022 to 2026. Earlier, the global chicory market chicory exports were limited to $ 0.48 million in 2003-04, but they rose to $7.49 million in 2013-14, a 32% increase. The total values in export for chicory in India were $ 17,268, $ 16,849, $ 14,973 and $ 16,366 in 2016, 2017, 2018 and 2019, respectively. The prices of chicory in India per tonne for the years 2016, 2017, 2018 and 2019 were $ 915.01, $ 932.02, $ 825.41 and $ 774.65, respectively. In 2022, the approximate price range for India, chicory is between $ 0.77 and $ 0.83 per kilogram or between $ 0.35 and $ 0.38 per pound. The price in Indian Rupee is INR 58.11 per kg. The average price for a tonne is $774.65 in Mumbai and New Delhi. Indian chicory is exported in more than 54 countries. The value of chicory export from India in 2020 was $0.73 million $13.81 thousand during 2021 exported to United States. Major countries where chicory was exported in 2020 are South Africa ($0.3 million), Belgium ($0.1 million), France ($0.1 million), Portugal ($0.06 million), Malaysia ($0.05 million) (www.marketsandmarkets.com).

Chicory usage in India has yet to reach its full potential. Chicory is mostly used to blend with coffee, but it is also utilized as a coffee supplement in southern states such as Kerala and Tamil Nadu. Several leading Indian brands like Nestle, The chai company, Rage, urban platter are already using chicory in their coffee blend. More branding is required to encourage usage.

### 4.5 Economical botanical aspect

The US imports more than 2.3 million kgs of chicory blanched buds and 1.9 million kilos of roasted chicory roots for coffee, as reported by the US Commerce Department and tariff and trade data from 2002 (Schmidt *et al.*, 2007). According to a market research report, the US chicory market is forcasted to achieve $5.09 billion by 2026. The chicory business is highly growing and demanding. The globe chicory business currently has a large number of enterprises making chicory products. Beneo, Cosucra, Sensus, and Leroux are the major market players. These four firms accounted for 85.02 per cent of global output. Chicory's global consumption value rises at a 6.13 per cent average annual growth rate. Europe is the major consumer region because of the higher demand for downstream applications. In 2016, this region accounted for 53.91 percent of the global consumption volume. Chicory goods are primarily divided into three categories: chicory flour, roasted chicory, chicory inulin, and others. And, in turn, each type has its own set of industries. Because of chicory's medicinal properties and flavor, downstream businesses will require more chicory products. As a result, chicory has a significant future market potential. Manufacturers in the business are attempting to improve technology in order to manufacture high-performance chicory (www.market-research-reports.com). Belgium harvests over half of all global production, followed by France, Poland, the Netherlands, and South Africa. Chicory roots are harvested in fewer than 20 countries throughout the world.

**Table 1: List of chicory companies in india**

| S.No. | Company name | Location | Product |
|---|---|---|---|
| 1 | Anwel Life Sciences Pvt. Ltd | Bharuch, Gujarat | Instant chicory powder |
| 2 | Farmvilla Food Industries Pvt. Ltd | Ahmedabad, Gujarat | Instant chicory powder, roasted chicory |
| 3 | Organinc India Pvt. Ltd | Lucknow, Uttar Pradesh | Chicory cubes |
| 4 | Adept Intex Pvt. Ltd | Agra, Uttar Pradesh | Chicory root (dried and roasted), chicory leaves |
| 5 | Dynamic Agro International | Sidhpur, Gujarat | Dried chicory cubes, roasted chicory cubes, raw chicory cubes, instant chicory powder, liquid chicory extract |
| 6 | Ryot Chicory growers and suppliers | Mathura, Uttar Pradesh | Chicory (dried, roasted and granular) |
| 7 | Shanmugavel Chicory industries | Tamilnadu | Chicory powder, roasted chicory root |
| 8 | Mahi exports, India | Gujarat | Chicory cubes and powder |
| 9 | Pioneer chicory | Gujarat | Chicory (dried, roasted), chicory extract, instant chicory powder |
| 10 | Vashila Agro Industries | Ahmedabad, Gujarat | Chicory powder |
| 11 | Perennial Life Sciences Pvt.Ltd | Mukherjee Nagar, New Delhi | Instant chicory powder, roasted chicory powder, roasted chicory powder extract, |
| 12 | Shiv Krishna Chicory Processing | Etah, Uttar Pradesh | Chicory (hand dice and machine dice) |
| 13 | Vindhya Trade Nest | Lucknow, Uttar Pradesh | Chicory root |
| 14 | GD Foods and Beverages Pvt. Ltd | Chennai, Tamilnadu | Spray dried instant chicory |
| 15 | R.S Chicory India Pvt. Lmt | Mathura, Uttar Pradesh | Hand cut chicory, chicory (dried, roasted , liquid and instant) |
| 16 | Vstexim | Mannargudi, Tamilnadu | Chicory powder (roasted, instant, instant granulated) |
| 17 | Chicory India | Vadodara, Gujarat | Chicory roasted powder, chicory roasted cubes, spray dried chicory powder and liquid |
| 18 | Ambe Phytoextracts Pvt. Ltd | Shakarpur, Delhi | Chicory cubes (roasted, dried), instant chicory powder |
| 19 | R.K Agroexport Pvt. Ltd | Noida, Uttar Pradesh | Chicory (powder, cube, extract, instant powder, root, roasted grains, liquid) |
| 20 | Prism Industries Ltd | Gujarat | Chicory root powder |
| 21 | Imperial Malts Ltd | Gurgaon, Haryana | Chicory extract powder |
| 22 | Karma Group | Shastri Nagar, Delhi | Chicory seed |
| 23 | S.L.N Coffee Pvt. Ltd | Kushalnagar, Karnataka | Instant chicory coffee |
| 24 | Dutt Exim | Gujarat | Chicory |
| 25 | S.V Agro Food | Navi Mumbai, Maharashtra | Chicory seed powder |
| 26 | V.R Coffee Associate | Hyderabad, Telangana | Instant chicory powder |
| 27 | Neeraj Enterprises | Hyderabad, Telangana | Chicory seeds |
| 28 | Delecto Foods Pvt. Ltd | Secunderabad, Telangana | Chicory seeds, chicory powder coffee, chicory extract powder, roasted chicory powder, instant chicory powder, chicory root powder |
| 29 | Jamnagar chicory industries | Jamnagar, Gujarat | Chicory cubes (roasted and dried), liquid chicory |
| 30 | Bioprex lab | Pune, Maharashtra | Instant chicory powder |

## 5. Phytochemistry

### 5.1 Nutritional value

Fresh chicory root ideally constitutes 68% inulin, 14% sucrose, 5% cellulose, 6% protein, 4% ash, and 3% other compounds by dry weight. Dried chicory root extract composed of roughly 98% inulin and 2% other compounds by weight (Kim and Shin, 1996). Root of fresh chicory may constitute almost 13 to 23% inulin, a polysaccharide equivalent to starch, by total weight (Wilson *et al*., 2004).

Fructose content in chicory is high; approximately 94%. It is a preserved carbohydrate contains upto 22-60 fructose molecules in a chain, having glucose molecule at the tail. Chicory roots have been used to extract fructans (Nandagopal and Kumari , 2007). The seeds are rich in volatile compounds and other bioactive compounds, while the corola provide a glucoside that is colourless until it is washed with alkalies giving a golden yellow colour.

### 5.2 Bioactive compounds

The existence of various beneficial chemicals in different sections of chicory is confirmed by phytochemical research. Sesquiterpene lactones, some derivatives of caffeic acid, inulin, sugars, proteins, hydroxycoumarins, flavonoids, alkaloids, steroids, terpenoids, oils, volatile compounds, coumarins, vitamins and polyynes (Fleming, 2000; Nandagopal and Kumari, 2007; Mushtaq *et al*., 2013; Shad *et al*., 2013).The compounds 18 alpha, 19 beta-20(30)-taraxasten-3beta, 21alpha-diol (cichoridiol) and 17-epi-methyl-6-hydroxy-angolensate (intybusoloid), lupeol, friedelin, beta-sitosterol, stigmasterol, betulinic acid, betulin, betulinaldehyde, syringic acid, vanillic acid) 6,7-hydroxycoumarin, and methyl-alpha-D-galactopyranoside were obtained from the methanolic extract of seeds of *C. intybus (*Zareen *et al*., 2008; Ahmed *et al*., 2008).

A new compound, cichotyboside, isolated from the seeds of *C. intybus* which was characterized as 2 alpha, 6 beta, 7 beta,15-tetrahydroxy-1 (10), 4 (5)-diene-guaian-9alpha, 12-olide-7-O-beta-caffoyl-15-O-beta-D-glucoside (Ahmed *et al*., 2008). There are various volatile compounds present in the *C. intybus* plant such as, octane, 2-pentyl furan, (2E, 4E)-Heptadienal, benzene acetaldehyde, n-nonanal, (*E*)-caryophyllene, geranyl acetone, sesquicineole, (*E*)-2-hexylcinnamaldehyde, (2*E*)-tridecanol, (5*E*, 9*E*)-farnesyl acetone, (2*E*)-undecanol acetate, 1,8-cineole, beta-elemene, n-eicosane, n-nonadecane, n-octadecanol (Judžentienė and Būdienė, 2008). A few pharmacologically important bioactive compounds including lactones, flavonoids, sterols, polyphenols responsible for anti-inflammatory, anticancer and antidiabetic (Al Snafi, 2016) have been shown in the Figure 3 and a list of bioactive compounds found in *C.intybus* is shown in Table 2.

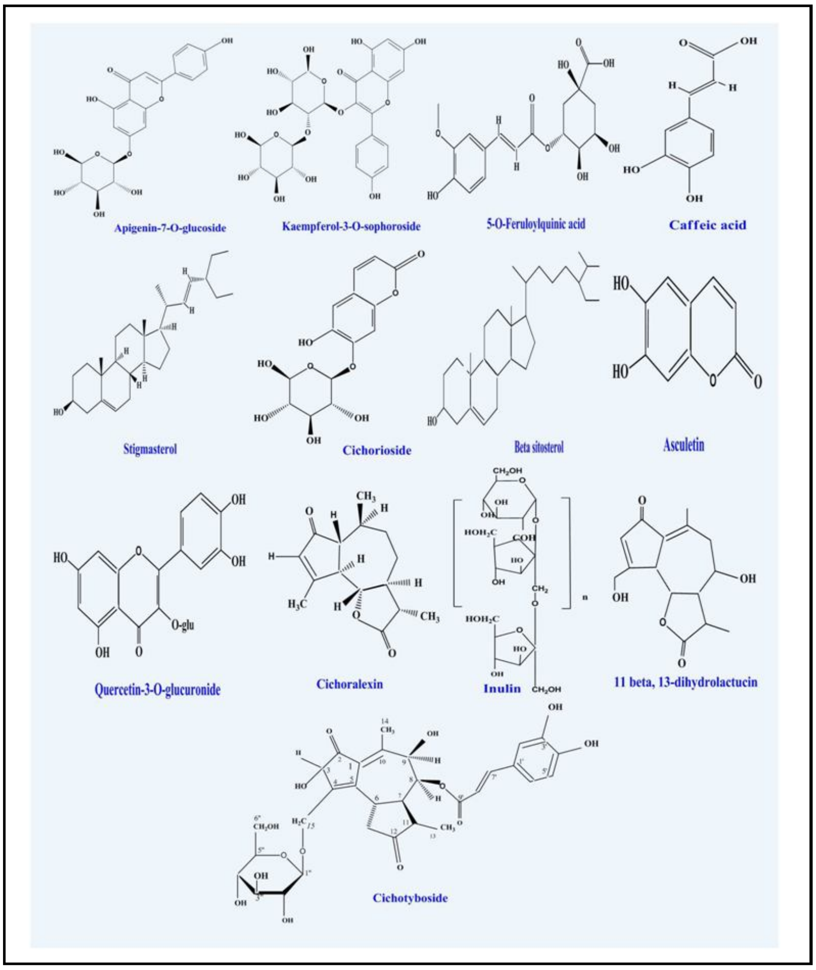


**Figure 3: Important bioactive compounds of *C. intybus*.**

Flavonoids, Terpenoids, saponins, Tannins, cardiac glycosides, and anthocyanins were found in each portion of the *C. intybus* (root, stem, leaves, and seeds) during phytochemical screening. Saponin levels were discovered to be high in seeds, while TF and TPA levels were found to be relatively high in leaves.

The chemical composition of chicory root, peel, seed, and leaf ethanol extracts, particularly their inulin and phenolic fractions, has been determined. The leaf extract as well as the seed extracts showed smaller inulin content (1.7 and 3.2 g per 100 g of fresh mass, respectively) and greater phenolic content (9.6 and 4.22 g per 100 g of fresh mass, respectively), which were identified as caffeoylquinic acids, chicoric acid, and quercetin glucuronide (Jurgonski *et al.*, 2011). Total phenolic content (50.8-285 GAE mg per 100 g dry plant matter) and total flavonoid content (43.3-150 CE mg/100 g dry plant matter) were both high in seeds extract of *C. intybus* (Mehmood *et al.*, 2012).

**Table 2: Bioactive constituents of *C. intybus***

| Compound name | Reference |
|---|---|
| Lactucin, Lactucopicrin, 8-Deoxylactucin Jacquilenin, 11 beta, 13-Dihydrolactucin, 11, 13-Dihydrolactucopicrin, Magno-lialide, Crepidiaside B; Ixerisoside D; Loliolide; Cichorioside B; Sonchuside A; Artesin; Cichoriolide ; Cichorioside; Sonchuside C; Cichopumilide | Bischoff *et al.*, 2004; Leclercq, 1984; Kisiel and Zielinska, 2001, Kisiel and Zielinska, 2001 |
| Cyanidin3-O-p-(6-O-malonyl)-Dglucopyranoside; 3,4 beta-Dihydro-15-dehydrolac tucopicrin; Cyanidin 3-O-β-(6-O-malonyl)-D-glucopyranoside | Bridle *et al.*, 1984 |
| Putrescine; Spermidine; Campesterol; beta-Sitosterol | Krebsky *et al.*, 1999; Süntar *et al.*, 2012 |
| (7S,8R)-32 -Demethyl-dehydrodiconiferyl alcohol-32-O-β-glucopyranoside;3,5-Dicaffeoylquinic acid ;4,5- Dicaffeoylquinic acid; Crepidiaside A; Chlorogenic acid | Malarz *et al.*, 2013; Norbaek *et al.*, 1990; Tousch *et al.*, 2008 |
| Cichoralexin | Monde *et al.*, 1990 |
| Delphinidin 3,5-di-O-(6-O-malonyl-β-D-glucoside); Delphinidin 3-O-(6-O-malonyl-β-D-glucoside)-5-O-β-D-glucoside;Delphinidin3-O-β-D-glucoside-5-O- (6-O-malonyl -β-D-glucoside); Delphinidin 3,5-di-O-β-D-glucoside; 3-O-p-Coumaroyl quinic acid; Quercetin 3-O-β-D-glucoside | Norbaek *et al.*, 2002 |
| Oxalic acid; Shikimic acid; Quinic acid; Succinic acid Malic acid; 3-Caffeoylquinic acid; 5-Caffeoylquinic acid; 4-Caffeoylquinic acid; *cis*-5-Caffeoylquinic acid; *cis*-Caftaric acid; *trans*-Caftaric acid; 5-Caffeoylshikimic acid; 5-*p*-Coumaroylquinic acid; Quercetin -3-O-glucuronide-7-O-(622 - O-malonyl)-glucoside; Kaempferol-3-O-glucosyl-7-O-(62 2-O-malonyl)-glucoside; Dimethoxycinnamoyl shikimic acid; Kaempferol-3-O-sophoroside; Dicaffeoyltartaric acid (chicoric acid)Kaempferol-7-O-glucosyl-3-O-(622 -malonyl)-glucoside; Delphinidin-3-O-(62 2 -O-malonyl)-glucoside-5-O-glucoside; Cyanidin-3,5-di-O-(62 2 -O-malonyl)-glucoside; Cyanidin-3-O-(62 2 -O-malonyl)-glucoside; Petunidin-3-O-(62 2 -O-malonyl)-glucoside; Cyanidin-3-O-galactoside; Cyanidin-3-O-(62 2 -O-acetyl)-glucoside; Malvidin-3-O-glucoside; Pelargonidin-3-O-monoglucuronide; 4-O-Feruloy-lquinic acid; Apigenin-7-O-glucoside; Chrysoeriol-3-O -glucoside; | Papetti *et al.*, 2013 |
| Tricin-3-O-glucoside; 1,3-Dicaffeoylquinic acid; 1,4-Dicaffeoylquinic acid; 3,4-Dicaffeoylquinic acid; Quercetin-7-O-galactoside; Quercetin-3-O-(6-0-O-malonyl)-beta-D-Glucoside; Quercetin-7-O-glucoside; Quercetin-7-O-glucuronide;Quercetin-7-O-(6''-O-acetyl)-glucoside; Kaempferideglucuronide; Kaempferol-7-O-glucoside; Kaempferol-7-O-rutinoside; Quercetin-7-O-p-coumaroylglucoside; Isorhamnetin-7-O-neohesperidoside; Kaempferol-7-O-(62 2 -O-malonyl)-glucoside; Kaempferol-7-O-glucuronide; Kaempferide-3-O-(62 2 -O-malonyl)-glucoside; Kaempferol-3-O-glucuronide; Kaempferol-3-O-glucuronide-7-Oglucoside; Kaempferol-3-O-(62 2 -O-malonyl)-glucoside; Kaempferol-3-O-glucoside; Myricetin-7-O-(62 2 -O-malonyl)-glucoside; Kaempferol-7-O-neohesperidoside; Kaempferol-7-O-(62 2 -O-acetyl)-glucoside; Kaempferol-3-O-(62 2 -O-acetyl)-glucoside; Isorhamnetin-7-O-glucoside ; Isorhamnetin-7-O-glucuronide; Caffeic acid; Cyanidin; Cyanidin-3-O-glucoside | Carazzone *et al.*, 2013; Tousch *et al.*, 2008; Bridle *et al.*, 1984. |

## 6. Biological and pharmacological activities

### 6.1 Antimicrobial activity

The experimental study revealed that antibacterial activity of chicory extract is different in gram-positive in comparison to gram-negative. gram-positive bacteria were shown to be more susceptible to chicory extracts compared to gram-negative bacteria, possibly due to gram-negative bacteria's hydrophilic cell walls included lipopolysaccharide, which prevented the phenolics compounds to accumulate in the cell membrane (Kilani *et al.*, 2008).

The evaluation of antimicrobial activity of methanolic extract and fractions of different solvent (n-butanol, ethyl acetate, chloroformand n-hexane) of chicory seeds were evaluated against a series of bacterial and fungal strains. Evaluation of antimicrobial potential was done by the disc diffusion assay and minimum inhibitory concentration (MIC) method. The antibacterial activity of *C. intybus* seeds fraction was moderate while results of antifungal evaluation showed that *C. intybus* seeds extract was mild for *R. solani* and very low for *A. flavus* and *A. niger* (Mehmood *et al.*, 2012). Polyphenols, tannins, and coumarins present in crude extracts of herbal plants may also have a role in antibacterial action (Petrovic *et al.*, 2004). Chicory root extracts in water, ethanol, and ethyl acetate were found to have effective antibacterial potential when tested against *S. aureus, S. typhi, B. thuringiensis* and *E.coli* and in certain research, the inhibitory activity of chicory root extract against *E. coli* has not been verified (Bajpai *et al.*, 2009).

Penicillium and Aspergillus species of fungus were the most susceptible against every extracts. There was no inhibitory activity observed against *Penicillium* sp. and *Aspergillus* sp. Inhibitory activity was seen against *Pseudomonas fluorescens, Agrobacterium tumefaciens,Pseudomonas aeruginosa, Erwinia carotovora, Sarcinalutea*, zoophilic and anthropophilic dermatophytes (Mares *et al.*, 2005). Phenolic chemicals can influence the permeability of cell walls and cell membranes, allowing the discharge of intracellular components and interfering with the microbe's membrane functionality (Signoretto *et al.*, 2011). Cell division, DNA, and RNA production, as well as the elongation of *Prevotella intermedia* cells, may be inhibited by aqueous extract of red chicory (Hassan *et al.*, 2010).

### 6.2 Antioxidant activity

Chicory has shown remarkable potential as an essential agent for reducing oxidative stress and hepatic damage caused by nitrosamine chemicals (Lante *et al.*, 2011). The potential of red chicory leaf as an innate alternative to commercial antioxidants in the food and feed industry was investigated. In the Rancimat test, it actively stayed stable after lyophilization and lowered LPO of several oils. Red chicory extract was also found to have a pleiotropic beneficial influence on stress-responsive genes when given to yeast culture before oxidative stress induction (Lavelli, 2008).

*C. intybus* var. *silvestre* were explored to see if there was a link between their polyphenol concentration and antioxidant activity. The total amount of phenolics was found to be substantially linked with antioxidant activity, when examined with both synthetic radical reactions as well as enzyme-catalyzed reactions (Ali, 2012). In diabetic rats, vanadium combined with chicory leaves had a significant impact on glucose metabolism and antioxidant state (Kim, 2002). Chicory leaf extract also exhibited improved antioxidant system activation, which protects the heart (Nayeemunnisa, 2003).

The antioxidant activities of *C. intybus* were examined *in vitro* and hepatoprotective activity against liver tissues of rats microsome lipid peroxidation was evaluated by 2-thiobarbituric acidreactive compounds produced by peroxide degradation. The antioxidant activity and hepatoprotective activity of all the vegetable juices was high but variable (83%, 64%). The vegetable included both biological antioxidant and pro-oxidant chemicals, as shown by dialysis and fraction analysis (Gazzani *et al.*, 2000).

The aqueous extract of *C. intybus* exhibits antioxidative and inhibitory effects on LDL, as well as thiobarbituric acid reactive material production and fatty acid breakdown (D'evoli *et al.*, 2013). Due to antioxidant activity, the presence of a significant number of anthocyanins in *C. intybus* seeds may have a direct scavenging effect on the production of reactive oxygen species (ROS) (Cavin *et al.*, 2005).

### 6.3 Anti-inflammatory activity

Root of *C. intybus* subjected to alcoholic extraction were found to exhibit anti-inflammatory properties for treating pyorrhea and gingival irritation (Papetti*et al.*, 2013). Chicory not only protected ethanol-induced immunotoxicity, but it also had anti-inflammatory characteristics (Rizvi *et al.*, 2014).

Roots of chicory also showed anti-inflammatory effectiveness in a carrageenan-induced paw edema model in a concentration-dependent manner. It reduced IL-1, TNF- alpha and IL-6levels in the blood, as a result it enhanced antioxidant potential of the paw tissue. Thus, indicating that chicory roots' anti-inflammatory and antioxidant properties are mediated through cytokine suppression (Ahmed *et al.*, 2009). In obese mice, the combination of *Origanum majorana* and *C. intybus* extract were reported to diminish body weight, boost liver function, total cholesterol and thyroid action (Rub *et al.*, 2009).

HT29 cells (human colon cancer cells) treated with the pro-inflammatory drug TNF-alpha, ethyl acetate fraction of chicory root extract inhibited the synthesis of prostaglandin E2 (PGE2). Two distinct mechanism of action have been discovered: (1) a considerable inhibition of cyclooxygenase 2 (COX-2) protein expression induced by TNF-alpha, and (2) a direct inhibition of COX enzyme activities with a significantly higher selectivity for COX-2 activity. The inhibition of TNF-alpha-dependent COX-2 expression was accomplished *via* inhibiting NF-kappa B activation. The guaianolide 8- deoxylactucin, a prominent sesquiterpene lactone found in chicory root, has been identified as the primary inhibitor of COX-2 protein expression in chicory extract (Cavin *et al.*, 2005).

A placebo-controlled, double-blind, dose-escalating experiment was done in patients with osteoarthritis to investigate the efficacy and suitability of chicory root extract (OA). This findings revealed that chicory root extract could be useful for treatingoste oarthritis. Just one patient who received the maximum dosage of chicory extract, stopped taking it because of side effects (Olsen *et al.*, 2010).

### 6.4 Antidiabetic activity

Radiolabelled glucose absorption and lipid accumulation tests were used to investigate the transportation of glucose and adipocyte tissues development in 3T3-L1 cells to observe the effectiveness of *C. intybus* methanolic extract. Chicory methanolic extract increased glucose absorption significantly and in a dose-dependent manner. Preadipocyte differentiation was also suppressed (Ghamarian *et al*., 2012). The chicory root which is rich in polyphenol fraction has a significant hypoglycemia potential because of its antioxidant potential (Pushparaj *et al*., 2007). Shortterm and long term effects of aqueous extract of chicory seed on diabetes were observed. Chicory may be effective as a natural dietary supplement for slowing diabetes (Ghamarian *et al*., 2012). This was corroborated by a study that found that giving STZ-induced diabetic rats at dose of 500 mg $kg^{-1}$ of *C. intybus* seed extract for 21 days exhibited a sustained anti-hyperglycemic effect (Kaskoos, 2012). A chicory seed extract high in caffeoylquinic acid reduced diet-induced metabolic abnormalities in type 2 diabetes (Jurgoński *et al*., 2011).

In Streptozotocin (STZ) treated rats alone, an intraperitoneal injection of *C. intybus* extract lead to a remarkable reduction in blood glucose, cholesterol and malondialdehyde level, as well as increased the level of reduced glutathione, superoxide dismutase (SOD), glutathione-S-transferase (GST), and catalase (CAT) activities. According to these findings, the *C. intybus* extract (Samarghandian *et al*., 2013) has antioxidant capabilities and prevents diabetic complications by modulating the oxidative stress system. Chicory could treat hyperglycemia (high blood sugar), hyperlipidemia (high cholesterol), insulin resistance, nonalcoholic fatty liver disease (NAFLD), and nonalcoholic steatohepatitis all at the same time, possibly by modulating the ratio of peroxisome proliferator-activated receptor-alpha to sterol receptor element-binding protein-1 (Ziamajidi *et al*., 2013).

Incorporating chicory root extract (CRE)/inulin into the diet reduced glucose absorption in the jejunum (Kim and Shin, 1996). These findings also indicated that consumption of CRE in tea could be useful for both diabetics and non-diabetics, particularly for postprandial hyperglycemia by reducing glucose absorption in the intestine.

Ethanolic extract of chicory was studied for its antidiabetic action on streptozotocin (STZ) treated male SD rats. The glucose tolerance test was altered (125 $mgkg^{-1}$ body weight) orally, and the same dose taken orally for 14 days lowered serum glucose by 20% and cholesterol by 16%. During the investigation, there was no significant changes in insulin secretion (Nishimura *et al*., 2015). However, Tousch *et al*. (2008) studied that chicoric acid isolated from chicory plant which is a type of caffeoyl ester, improved glucose transport and insulin secretion, implying that it could be used as a type 2 diabetes medication that affects both insulin sensitivity and secretion. The exact cause of contradictory inspection is unknown.

In a randomized, double-blind, placebo-controlled trial, 47 adult healthy volunteers were separated into a test group who were administered orally, chicory root extract and a placebo group who were given barley tea at a rate of 300 ml daily for 4 weeks. Chicory root extract had positive effects such as antihyperglycemic and antidyslipidemic effects, as well as better bowel movement (Nishimura *et al*., 2015).

## 6.5 Hepatoprotective activity

Chicory's traditional use as a hepatoprotectant is widely documented. Oral doses of chicory ethanolic extract given at the rate of 6, 18, and 54 mg/kg BW per day reduced liver enzymes and had a substantial hepatoprotective effect (aspartate transaminase and alanine transaminase). The results showed promising effect when given at a daily dosage of 54 $mgkg^{-1}$ BW (Li *et al*., 2014).

Aqueous and methanolic extract of chicory were given intraperitoneally to albino rats, which resulted in a significant reduction in liver enzymes (Gadgoli and Mishra, 1997). Hepatoprotective activity of chicory was proven in lowering blood ALT and AST levels below the normal range after long-term treatment (Helal *et al*., 2011). Furthermore, a combination of *C. intybus* and *Cinnamon zeylanicum* extract shown to be useful in NAFLD patients by reducing liver enzymes (Asl *et al*., 2014). *C. intybus* contains antioxidants, phenolics, and alkaloids that have a substantial hepatoprotective effect (Saggu *et al*., 2014).

In HepG2 cells, hydrogen peroxide-induced toxicity was tested by hydroalcoholic fraction of chicory leaves. The harmful effect was recovered by hydroalcoholic portion of *C. intybus* leaves extract (Neha *et al*., 2014). The efficacy of chicory leaves aqueous extract alone or in combination with aqueous extract of dandelion leaves was seen against carbon tetrachloride-induced hepatotoxicity in wistar albino rats demonstrated hepatoprotective effects with significant reductions in liver enzymes levels (Al Malki and Abo Golayel, 2013). The dietary intake of a premix of celery leaves, chicory leaves, and barley grains together proved to be hepatoprotectant and hypolipidemic agent, reducing liver enzymes and improving cholesterol levels in hypocholestrolemic rats. A study found that a increased amount of extract (200 mg/kg/B.W, intraperitoneally in rats) had a hepatotoxic impact, contradicting the conventional belief in the hepatoprotective function of *C. intybus* leaves extract. The hepatoprotective effect of seed ethanolic extract had a strong effect against carbon tetrachloride-induced toxicity, which might be due to individual alone or the combined effect of bioactive compounds found in them. This finding backs up the legendary claim of *C. intybus* seeds as a hepatoprotective therapy (Jamshidzadeh, 2006). A methanol extract of chicory seeds was found to have a substantial anti-hepatotoxic effect and is important constituent in Jigreen, an Indian commercial medicine for the treatment of various liver ailments (Ahmed *et al*., 2008). Aqueous extract of chicory root and callus was administered orally and its hepatoprotective effect was observed in albino rats. Furthermore, histological analysis of the liver after treatment revealed no fat buildup or necrosis (Zafar and Ali, 1998).

Chicory's hepatoprotective effects were attributed to its ability to prevent lipid peroxidation, support endogenous antioxidants, and upregulation of genes encoding antioxidant enzymes, all of which helped to prevent DNA damage. It is due to specific antioxidant found in roots of chicory, significantly reducing oxidative stress and induced hepatic disorders (El-Sayed *et al*., 2015).

In rats, hepatotoxicity was induced by administration of paracetamol (640 mg kg-1) orally, as evidenced by increased AST, ALT and ALP serum enzyme levels. The paracetamol-induced elevation in serum enzymes was reduced by pretreating rats with esculetin (6 mg/kg). The $CCl_4$ induced liver toxicity when administered orally at a dosage of 1.5 ml/kg, also increased serum levels of ALT, AST and ALP. The $CCl_4$-induced toxicity resulting elevation in serum enzymes was hampered by the same dose of esculetin (6 mg/kg). Esculetin also reduced $CCl_4$-induced pentobarbital sleeping time extension, indicating hepatoprotective.

The presence of esculetin in *C. intybus* and *Bougainvellae spectabillis* could elucidate the folklore utilization of these herbs in hepatic injury (Gilani *et al.*, 1998).

A study investigated the antihepatotoxic effects of *C. intybus* natural root and root callus extracts in albino rats against carbon tetrachloride-induced liver damage. They discovered that both the *C. intybus* root callus extract and the natural root extract were protective against carbon tetrachloride-induced hepatocellular damage, but that the *C. intybus* root callus extract was more protective than the natural root extract (Zafar and Ali, 1998).

A study explored the antioxidant properties of aqueous extract of *C. intybus* var. *silvestre in vitro* and *in vivo* against rat liver cell microsome lipid peroxidation. It was found that the plant comprises of both biological antioxidant and pro-oxidant compound and the (AA), (PA) showed high, but very variable AA (>83%) and PA (>64%) (Gazzani *et al.*, 2000).

In rats with $CCl_4$-induced hepatitis, *C. intybus* root extract normalized some morphofunctional liver aspects such as it decreased level of glycogen, cell necrosis and increased the number of protein synthesising cells (Krylova *et al.*, 2006).

*C. intybus* was tested for polyphenol content using the Folin-Ciocalteu method in 10 *Lactuca sativa* genotypes, one of which was *C. intybus*. The reaction with the stable DPPH* radical was used to determine the antiradical activity. The maximum polyphenol content was found in a farmed *C. intybus* cultivar, while the best antiradical activity was found in a wild *C. intybus* genotype (Heimler *et al.*, 2007). *C. intybus* seeds were shown to contain cichotyboside, which has an antihepatotoxic effect against $CCl_4$-induced hepatotoxicity in wistar rats, lowering ALP, ALT, and AST levels while boosting total albumin levels to levels comparable to intoxicated controls (Jurgońskiet *al.*, 2011). In addition, Ahmed *et al.* (2003) investigated the antihepatotoxic efficacy of the chemical AB-IV from *C. intybus* alcoholic extract on $CCl_4$ induced hepatotoxicity in albino rats. The antihepatotoxic activity of the chemical AB-IV was comparable to that of silymarin, a conventional medication. The histopathological observation depicts almost complete homogenization of the tissues as there was no fatty acid accumulation and necrosis was observed by AB-IV compound (Ahmed *et al.*, 2003).

Chicory and ginger were combined in a study to investigate, if they had a hepatoprotective impact. To evaluate the hepatoprotective effect against carbon tetrachloride intoxication in rats, they administered ginger, chicory, and their mixture at doses (250 and 500 mg/kg) alone or blended (1:1 wt by wt). The results demonstrated that the extract of chicory reduced (AST), (ALT), and (ALP), indicating that the plant could protect the liver from acute injury (Atta *et al.*, 2010). *C. intybus* was evaluated as a supplementary diet for hepatoprotection against nitrosamine by a group of researchers. The rats given nitrosamine had significantly higher levels of liver cholesterol, bilirubin, lipids and enzyme activity (ALT, ALP, AST, and gamma glutathione) in both blood and liver. In the group, there was a significant drop in SOD, catalase, GSH, and GSH-Rx levels. They also discovered that the plant was successful in modulating the reported nitrosamine anomalies, as evidenced by improvements in the tested biochemical and antioxidant parameters components. In conclusion, chicory reduces oxidative stress and liver damage (Hassan and Yousef, 2010).

An assessment of the antioxidant various solvent extracts of (*C. intybus*) leaves were tested *in vitro*. Aqueous extract of *C. intybus* possessing the phenolic compounds was found to have considerable radical scavenging effects as well as significant protection against protein oxidation and DNA damage (Ilaiyaraja and Khanum, 2010).

A research study was conducted to see the combined impact of diet supplemented with barley, chicory and celery on liver enzymes and blood lipids in rats fed with a cholesterol-rich diet. It was either added separately at 10% for each plant or in a mixture of all three plants at 15% for four weeks. It was discovered that a diet supplemented with 10% of each of them reduced increased serum levels of liver enzymes and blood lipids, but that the combination of alltogether was more efficient in minimizing blood lipids and liver enzymes. Finally, it was suggested that patients with hypercholesterolemia and liver illness benefit from a dietary consumption of a plant mixture of chicory, barley and celery at a concentration of 15% (5%) of each (Abd El Mageed, 2011).

*Cichorium endivia* extract (CEE) was discovered to substantially reduce oxidative stress and cytotoxicity in HepG2 cells produced by tert-butyl hydroperoxide (t-BHP). The results showed a promising and protective impact by decreasing serum levels of ALT and AST and preventing changes in liver biochemistry such as GST, GSH, SOD, and MDA. As a result, they hypothesized that the phenolic compounds in CEE may be responsible for its safe treatment of liver illness (Chen *et al.*, 2011).

Aqueous-methanolic extract of *C. intybus* seeds were tested on acetaminophen and $CCl_4$-induced liver injury to see its hepatoprotective effect. In mice, acetaminophen caused 100 per cent mortality at a dose of 1 g per kg, but 500 mg per kg of plant extract resulted in increased mortality to 70% (Gilani and Janbaz, 1994).

Cichotyboside, isolated from the seeds of *C. intybus*, had noticeably showed effect against hepatotoxicity in wistar rats, by reducing the liver enzymes such as SGOT by 52 units/ml; SGPT 38 units/ml; ALKP 24.97 units/ml, with 7.54 g/dl, 5.48 g/dl. The levels of ALKP was reduced by 88% as compared to standard medicine silymarin which was 92%, and total albumin level when compared with the control sample was increased by 85% to silymarin's 89%. In comparison to the standard and controls, the SGOT and SGPT levels were significantly reduced (Ahmed, 2008).

### 6.6 Wound healing effect

The healing properties of *C. intybus* leaves, roots, aerial parts, together with ashes of either leaves or roots, were investigated *in vivo*. For the wound healing activity evaluation, tissues which contain hydroxyproline was treated with extract and the activity was measured. Furthermore, antioxidant activity was also evaluated by measuring scavenging activity and overall phenolic content to see whether it plays a role in wound healing or not. Anti-inflammatory evaluation was also examined by observing the inhibition of capillary permeability induced by increased acetic acid. One chemical was isolated *via* bioassay-guided fractionation, and its structure was determined using spectroscopic techniques. The fractions were analyzed for hyaluronidase, collagenase, and elastase enzyme inhibitory activities to determine the activity mechanisms. *C. intybus* root methanolic extract has been found to have potent wound healing properties. The results were promising when this extract was extracted with n-hexane, dichloromethane

(DCM), ethyl acetate, and n-butanol. DCM extract was the most active one and several class of compounds were fractionated from it by using chromatographic techniques and finally it was determined that the β-sitosterol is the major bioactive compound which is responsible for the wound healing activity (Suntar *et al.*, 2012).

### 6.7 Anticancer effect

Magnolialide, a 1-hydroxyeudesmanolide derived from the root part of *C. intybus*, was seen to inhibit many tumorous cells and seen to enhance monocyte or macrophage-like cell development in human leukemia HL-60 and U-937 cells (Lee *et al.*, 2000). On amelanotic melanoma C32 cell lines, an aqueous-alcoholic macerate of *C. intybus* leaves had an antiproliferative effect (Conforti *et al.*, 2008).

Aqueous extracts of *C. intybus* was tested against PC-3 cell line, T47D cells, and RKO cells to see its anticancer potential and it was observed that *C. intybus* extract showed a slight reduction of cell proliferation. At 1.0 to 10% concentration for 24 h, *C. intybus* (seeds) inhibited cell viability by 5-24 per cent (Nawab *et al.*, 2011).

Photosensitive chemicals such as lactucopicrin, anthocyanins, cichorin, and lactucin, were found in chicory. The therapeutic effect of chicory against DMBA induced benign breast cancers was examined. Chicory extract significantly increased P. carbonyl and malondialdehyde levels (MDA) while decreasing total antioxidant capacity and superoxide dismutase (SOD) levels. It also reduced the number of estrogen receptors ER-positive cells in tumor masses considerably (Al-Akhras *et al.*, 2012).

## 7. Other pharmacologically important activities

Aqueous extract of chicory root reduced cholesterol absorption in the jejunum by 30% and the perfused ileum by 41% (Kim, 2000). Chicory n-hexane extract had powerful anticancer and anti-proliferative action against Jurkat cells (Saleem *et al.*, 2014). The dendritic cell's T-cell stimulating capacity was investigated using an ethyl acetate preparation of chicory root. Dendritic cells' T-cell boosting function is inhibited at greater doses, whereas cytokine release is shifted to a TH1 pattern at lower values. The traditional use of this herb in the therapy of immune-mediated diseases was explained by these findings (Karimi, 2014). Chicory root extract was found to be effective in the treatment of osteoarthritis (Olsen *et al.*, 2010). Consumption of chicory coffee reduced the plasma as well as whole blood viscosity, and serum macrophage migration inhibitory factor levels, after a week (Schumacher*et al.*, 2011). Chicory leaves used heterologous production of total RNA to maintain calcium levels (Debarbieux *et al.*, 1999). Furthermore, inulin has been shown to improve calcium absorption (Abrams *et al.*, 2005). Guaianolides, eudesmanolides, and germacranolides were found in chicory. Like other dietary fibres, inulin and oligofructose are also among them which aids in the process of producing short-chain fatty acids which is later absorbed and metabolized throughout the body.

## 8. Toxicity and side effects

Because of its lengthy history of usage, *C. intybus* was thought to be a safe medicine because till date there is no known adverse effect seen with the correct prescribed dose. Skin contact with the medication has the potential to cause sensitization (Fleming, 2000). This shows that no extract or any other evidence of toxicity was responsible in rats, for acute and subacute/subchronic oral toxicity (28 days) investigation (Schmidt *et al.*, 2007).

The bioluminescence inhibition test with *Vibrio fischeri* was used to assess the toxicity of *C. intybus* extracts. When the marine luminous bacteria *V. fischeri* is exposed to toxins, this bacterial assay detects the decrease in light emission. Because the tested extracts inhibited bioluminescence by less than 20%, *C. intybus* was supposed to be edible for human consumption (Conforti *et al.*, 2008).

A double-blind, placebo-controlled,dose-escalating experiment performed in patients with osteoarthritis to investigate the efficacy and suitability of chicory root extract (OA). This finding revealed that chicory root extract could be useful in the treatment of OA. Pateint who received the maximum dosage of chicory, stopped taking it because of side effects (Olsen *et al.*, 2010).

## 9. Future prospects

Chicory has always remained a resourceful plant that is susceptible to genetic alteration to this day, and there is growing interest shown by scientists to produce genetically modified chicory to generate higher revenues and open up new opportunities (Bais and Ravishankar, 2001). Due to less or more significant side effects than synthetic pharmaceuticals, interest in herbal treatment to safeguard one's health has grown recently all over the world (Ansari and Ahmad, 2019). Approximately, 8000 plant species are employed as medicinal herbs in India, accounting for over half of all higher flowering plant species. They contain a variety of spices and culinary plants that are today considered key pharmacological sources (Alam, 2019; Ansari and Ahmad, 2019; Sekeroglu, 2019). *C. intybus* is cultivated and used for a variety of purposes in many places of the world. It's frequently utilised for its medicinal and preventive properties, as well as for overall well-being. Because of its high levels of proteins, carbs, minerals, and phytochemicals, it is helpful to both animals and humans. More in depth study needs to back up the traditional use of this valuable plant. *C. intybus* is a well-known coffee substitute, and from ancient times diverse components of the plant, such as roots, flowers, leaves and seeds, have been used as herbal medicines. Inulin, a prebiotic fiber produced from roots of chicory, is an important dietary element because of their altering properties which modify physiological and biochemical processes which ultimately results in overall betterment of human health and a lower possibility of a variety of disorders in humans (Kaur and Gupta, 2002). Root extract of chicory has been demonstrated in trials to be useful in the treatment of osteoarthritis (Olsen *et al.*, 2010), to have antithrombotic and anti-inflammatory properties (Schumacher, 2011), and it is useful in the treatment of NAFLD (Abd El-Mageed, 2011**)**. *In vivo* studies of *C. intybus* seed extract revealed the antidiabetic, antithrombotic, antioxidative and hepatoprotective activity. Chicory inulin is used to monitor renal function and to deliver therapeutic drugs to the colon due to its low molecular weight, it is neither absorbed or processed by the kidney but is easily eliminated (Mensink *et al.*, 2015). Inulin can be chemically modified to deliver encapsulated therapeutic drug molecules. Drugs that would normally be absorbed early in the GI tract are now carried to the colon, where gut bacteria break down inulin and the chemical is released (Mensink *et al.*, 2015). To date, no comprehensive study and pathway has been carried out to determine the efficacy of *C. intybus* in various diseases. Nonetheless, the pharmacological potential of many of its constituents has not been completely investigated. Thus, more and more research findings is needed to support a detailed mechanism of action of various phytochemicals against several diseases. For the prevention of prevalent lifestyle problems, recognized allopathic medications are lacking. Incorporating the plant into therapeutic treatment could aid in the development of a comprehensive approach to the management of lifestyle issues that incorporates both indigenous and allopathic methods. Despite significant advances in the field of allopathy over the twentieth century, herbs continue to be a key source of medications in both contemporary and traditional medical systems around the world (Biradar, 2015). Nanotechnology based drug delivery approaches may be employed for the effective delivery of bioactive compounds to the target organ. *C. intybus* activity demonstrated in both *in vitro* and *in vivo* research supports its traditional usage in medicine.

## 10. Conclusion

*C. intybus* is a common plant with great potential. It undoubtedly deserves to be used more widely in medical practices and phytotherapy based treatments. The whole plant; seeds, flowers, root or leaves either in fresh and dried form, can be incorporated into daily diet. The versatile benefits of *C. intybus* extracts might make them aattractive alternative source for the pharmaceutical industry. It is a valuable source of various bioactives for food products especially because of the presence of inulin, sesquiterpene lactones and phenolic compounds in roots, leaves, seeds, and flowers. The most prevalent chemical discovered in chicory is inulin, which may be exploited to generate value-added food items. On the other hand, because industrial chicory processing focuses on the roots, there are huge amounts of wasted chicory by-products (leaves and peels) that might be exploited to isolate beneficial components such sesquiterpene lactones and polyphenols. In order to supply industry and ensure the valorization of chicory plant parts and the sustainability of final products enriched in the nutritional and functional bioactives of chicory, future developments in the optimization of the extraction of economically important bioactive compounds from chicory and their implementation from pilot to industrial scale are required.In conclusion, the chicory plant is a rich and promising raw material for the development of functional food itemsas well as the phytochemical isolation and research of chicory's biological activity have backed up documented indigenous knowledge about its diverse medicinal benefits. Thus, clearly suggesting the *C. intybus* as a promising prospective resource for functional foods, beverages and nutritional supplements along with its usage in phytotherapy.

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## Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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